Appl. No. 10/054,300 Response to Office Action mailed June 27, 2006

Amendments to the Claims:

Claim 1. (currently amended) A compound of formula (1) or a pharmaceutically acceptable salt thereof,

$$R^{1}O$$
 R^{2}
 R^{2}
 R^{2}

wherein[[,]] R¹ is the same or different[[,]] and each represents selected from the group consisting of a hydrogen atom, a protecting group for a hydroxy group in nucleic acid synthesis, a phosphoric acid group, a phosphoric acid group protected with a protecting group in nucleic acid synthesis,

[[or]] and a group represented by the formula -P(R^{4a})R^{4b}, wherein R^{4a} and R^{4b} are the same or different and each represents a hydroxy group, a hydroxy group protected with a protecting group in nucleic acid synthesis, a mercapto group, a mercapto group protected with a protecting group in nucleic acid synthesis, an amino group, an amino group protected with a protecting group in nucleic acid synthesis, an alkoxy group having 1-6 carbon atoms, an alkylthio group having 1-6 carbon atoms, a cyanoalkoxy group

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having 1-7 carbon atoms, or an amino group substituted by an alkyl group having 1-6 carbon atoms,

 \mathbb{R}^2 represents an azido group, an amino group, or a group represented by the formula -NH-R³, wherein R³ is the same or different and each represents selected from the group consisting of a protecting group for an amino group in nucleic acid synthesis, a phosphoric acid group, a phosphoric acid group protected with a protecting group in nucleic acid synthesis, or a group represented by the formula $-P(R^{4a})R^{4b}$, wherein R^{4a} and R^{4b} [[is]] are the same or different and each represents a hydroxy group, a hydroxy group protected with a protecting group in nucleic acid synthesis, a mercapto group, a mercapto group protected with a protecting group in nucleic acid synthesis, an amino group, an amino group protected with a protecting group in nucleic acid synthesis, an alkoxy group having 1-6 carbon atoms, an alkylthio group having 1-6 carbon atoms, a cyanoalkoxy group having 1-7 carbon atoms or an amino group substituted by an alkyl group having 1-6 carbon atoms,

B represents a purin-9-yl group or a 2-oxo-1,2-dihydropyrimidin-1-yl group each of which is optionally unsubstituted or substituted with 1 or more substituents selected from the group consisting of

halogen atom.

- a hydroxy group,
 a hydroxy group protected with a protecting group in
 nucleic acid synthesis,
 an alkoxy group having 1-6 carbon atoms,
 a mercapto group,
 a mercapto group protected with a protecting group in
 nucleic acid synthesis,
 an alkylthio group having 1-6 carbon atoms,
 an amino group,
 an amino group protected with a protecting group in nucleic
 acid synthesis,
 an amino group substituted by an alkyl group having 1-6
 carbon atoms,
 an alkyl group having 1-6 carbon atoms[[,]] and
- Claim 2. (currently amended) The compound according to claim 1, wherein \mathbb{R}^1 represents a hydrogen atom, an aliphatic acyl group, an aromatic acyl group, a silyl group, a methyl group substituted by 1 to 3 aryl groups, or a methyl group substituted by 1 to 3 aryl groups wherein the aryl rings thereof are substituted by a lower-alkyl group, a lower-alkoxy group, a halogen atom or a cyano group.
- Claim 3. (currently amended) The compound according to claim 1, wherein \mathbb{R}^1 represents a hydrogen atom, a silyl group, a methyl

group substituted by 1 to 3 aryl groups, or a methyl group substituted by 1 to 3 aryl groups wherein the aryl rings thereof are substituted by a lower-alkyl group, a lower-alkoxy group, a halogen atom or a cyano group.

Claim 4. (currently amended) The compound according to claim 1, wherein R¹ represents a hydrogen atom, <u>a</u> trimethylsilyl group, <u>a</u> t-butyldimethylsilyl group, <u>a</u> t-butyldiphenylsilyl group, <u>a</u> benzyl group, <u>a</u> triphenylmethyl group, <u>a</u> 4-methoxybenzyl group, <u>a</u> 4-methoxyphenyldiphenylmethyl group, a 4,4'-dimethoxytriphenylmethyl group, or <u>a</u> 4,4',4''-trimethoxytriphenylmethyl group.

Claim 5. (currently amended) The compound according to claim 1, wherein R² represents an azido group, an amino group, or a group represented by the formula -NH-R³, wherein R³ represents an aliphatic acyl group, an aromatic acyl group, a methyl group substituted by 1 to 3 aryl groups, a methyl group substituted by 1 to 3 aryl groups wherein the aryl rings thereof are substituted by a lower-alkyl group, a lower-alkoxy group, a halogen atom, or a cyano group, a silyl group, a phosphoramidite group, a phosphoryl group, a phosphoric acid group or a phosphoric acid group protected with a protecting group in nucleic acid synthesis.

Claim 6. (currently amended) The compound according to claim 1, wherein \mathbb{R}^2 represents an azido group, an amino group, or a group represented by the formula -NH- \mathbb{R}^3 , wherein \mathbb{R}^3 represents an

acetyl group, <u>a</u> trifluoroacetyl group, <u>a</u> benzoyl group, <u>a</u> benzyl group, <u>a</u> p-methoxybenzyl group, <u>a</u> tert-butyldiphenylsilyl group, a group represented by the formula $-P(OC_2H_4CN)$ (NCH(CH₃)₂), a group represented by the formula $-P(OCH_3)$ (NCH(CH₃)₂), a phosphonyl group, [[or]] a [[2-]]chlorophenyl[[-]] <u>2-chlorophenylphosphonic acid group</u> or a 4-chlorophenylphosphonic acid group.

Claim 7. (original) The compound according to claim 1, wherein \mathbb{R}^2 represents an azido group or an amino group.

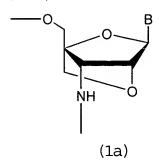
Claim 8. (original) The compound according to claim 1, wherein B represents 6-aminopurin-9-yl, 6-amino-purin-9-yl wherein the amino group is protected with a protecting group in nucleic acid synthesis, 2,6-diaminopurin-9-yl wherein one or both amino groups are protected with a protecting group in nucleic acid synthesis, 2-amino-6-chloropurin-9-yl, 2-amino-6chloropurin-9-yl wherein the amino group is protected with a protecting group in nucleic acid synthesis, 2-amino-6fluoropurin-9-yl, 2-amino-6-fluoropurin-9-yl wherein the amino group is protected with a protecting group in nucleic acid synthesis, 2-amino-6-bromopurin-9-yl, 2-amino-6-bromopurin-9-yl wherein the amino group is protected with a protecting group in nucleic acid synthesis, 2-amino-6-hydroxypurin-9-yl, 2-amino-6hydroxypurin-9-yl wherein the amino group is protected with a protecting group in nucleic acid synthesis, 6-amino-2methoxypurin-9-yl, 6-amino-2-methoxypurin-9-yl wherein the amino group is protected with a protecting group in nucleic acid synthesis, 6-amino-2-chloropurin-9-yl, 6-amino-2-chloropurin-9-yl

wherein the amino group is protected with a protecting group in nucleic acid synthesis, 6-amino-2-fluoropurin-9-yl, 6-amino-2fluoropurin-9-yl wherein the amino group is protected with a protecting group in nucleic acid synthesis, 2,6-dimethoxypurin-9yl, 2,6-dichloropurin-9-yl, 6-mercaptopurin-9-yl, 6mercaptopurin-9-yl wherein the mercapto group is protected with a protecting group in nucleic acid synthesis , 2-oxo-4-amino-1,2dihydropyrimidin-1-yl, 2-oxo-4-amino-1,2-dihydropyrimidin-1-yl wherein the amino group is protected with a protecting group in nucleic acid synthesis, 4-amino-2-oxo-5-fluoro-1,2dihydropyrimidin-1-yl, 4-amino-2-oxo-5-fluoro-1,2dihydropyrimidin-1-yl wherein the amino group is protected with a protecting group in nucleic acid synthesis, 4-amino-2-oxo-5chloro-1,2-dihydropyrimidin-1-yl, 4-amino-2-oxo-5-chloro-1,2dihydropyrimidin-1-yl wherein the amino group is protected with a protecting group in nucleic acid synthesis, 2-oxo-4-methoxy-1,2dihydropyrimidin-1-yl, 2-oxo-4-mercapto-1,2-dihydropyrimidin-1yl, 2-oxo-4-mercapto-1,2-dihydropyrimidin-1-yl wherein the mercapto group is protected with a protecting group in nucleic acid synthesis, 2,4-dihydroxypyrimidin-1-yl, 2,4-dihydroxy-5methylpyrimidin-1-yl, 4-amino-5-methyl-2-oxo-1,2dihydropyrimidin-1-yl, or 4-amino-5-methyl-2-oxo-1,2dihydropyrimidin-1-yl group wherein the amino group is protected with a protecting group in nucleic acid synthesis.

Claim 9. (original) The compound according to claim 1, wherein B represents 6-benzoylaminopurin-9-yl, adeninyl, 2-benzoylamino-6-hydroxypurin-9-yl, guaninyl, 2-oxo-4-benzoylamino-1,2-dihydropyrimidin-1-yl, cytosinyl, uracilyl or thyminyl.

Claim 10. (previously presented) The compound according to claim 1, wherein the compound is 3'-amino-3'-deoxy-2'-0,4'-C-methylene-5-methyluridine.

Claim 11. (withdrawn - currently amended) An oligonucleotide analogue or a pharmaceutically acceptable salt thereof having 1 or more structural units represented by the following formula (1a),



provided that when the oligonucleotide has two or more structural units of formula (1a), each B is the same or different,

wherein B represents a purin-9-yl group or a 2-oxo-1,2-dihydropyrimidin-1-yl group which are optionally unsubstituted or substituted with a substitutent selected from the group consisting of:

- a hydroxy group,
- a hydroxy group protected with a protecting group in nucleic acid synthesis,
- an alkoxy group having 1-6 carbon atoms,
- a mercapto group,
- a mercapto group protected with a protecting group in

nucleic acid synthesis, an alkylthio group having 1-6 carbon atoms, an amino group,

an amino group protected with a protecting group in nucleic acid synthesis,

an amino group substituted by an alkyl group having 1-6 carbon atoms,

an alkyl group having 1-6 carbon atoms[[,]] and a halogen atom.

Claim 12. (withdrawn) The oligonucleotide analogue or a pharmaceutically acceptable salt thereof according to claim 11, wherein B represents 6-aminopurin-9-yl, 6-aminopurin-9-yl wherein the amino group is protected with a protecting group in nucleic acid synthesis, 2,6-diaminopurin-9-yl, 2-amino-6-chloropurin-9yl, 2-amino-6-chloropurin-9-yl wherein the amino group is protected with a protecting group in nucleic acid synthesis, 2amino-6-fluoropurin-9-yl, 2-amino-6-fluoropurin-9-yl wherein the amino group is protected with a protecting group in nucleic acid synthesis, 2-amino-6-bromopurin-9-yl, 2-amino-6-bromopurin-9-yl wherein the amino group is protected with a protecting group in nucleic acid synthesis, 2-amino-6-hydroxypurin-9-yl, 2-amino-6hydroxypurin-9-yl wherein the amino and hydroxyl groups are protected with a protecting group in nucleic acid synthesis, 6-amino-2-methoxypurin-9-yl, 6-amino-2-chloropurin-9-yl, 6-amino-2-fluoropurin-9-yl, 2,6-dimethoxypurin-9-yl, 2,6-dichloropurin-9yl, 6-mercaptopurin-9-yl, 2-oxo-4-amino-1,2-dihydropyrimidin-1yl, 2-oxo-4-amino-1,2-dihydropyrimidin-1-yl wherein the amino group is protected with a protecting group in nucleic acid

synthesis, 2-oxo-4-amino-5-fluoro-1,2-dihydropyrimidin-1-yl, 4-amino-2-oxo-5-fluoro-1,2-dihydropyrimidin-1-yl wherein the amino group is protected with a protecting group in nucleic acid synthesis, 4-amino-2-oxo-5-chloro-1,2-dihydropyrimidin-1-yl, 2-oxo-4-methoxy-1,2-dihydropyrimidin-1-yl, 2-oxo-4-mercapto-1,2-dihydropyrimidin-1-yl, 2-oxo-4-hydroxy-5-methyl-1,2-dihydropyrimidin-1-yl, 4-amino-5-methyl-2-oxo-1,2-dihydropyrimidin-1-yl, 5-methylcytosinyl), or 4-amino-5-methyl-2-oxo-1,2-dihydropyrimidin-1-yl wherein the amino group is protected with a protecting group in nucleic acid synthesis.

Claim 13. (withdrawn) The oligonucleotide analogue or a pharmaceutically acceptable salt thereof according to claim 11, wherein B represents 6-benzoylaminopurin-9-yl, adeninyl, 2-isobutylamino-6-hydroxypurin-9-yl, guaninyl, 2-oxo-4-benzoylamino-1,2-dihydropyrimidin-1-yl, cytosinyl, 2-oxo-5-methyl-4-benzoylamino-1,2-dihydropyrimidin-1-yl, 5-methylcytosinyl, uracinyl or thyminyl.

Claim 14. (withdrawn) A pharmaceutical composition comprising a pharmaceutically effective amount of a pharmacologically active compound together with a carrier therefore, wherein said pharmacologically active compound is an oligonucleotide analogue comprising two or more nucleoside units, wherein at least one of said nucleoside units is a structure of the formula (1a) of claim 11, or a pharmaceutically acceptable salt of said compound.

Claim 15. (original) A method for the prevention or treatment in a mammal of a disease preventable or treatable by the pharmacologically useful antisense activity of an oligonucleotide analogue or a pharmacologically acceptable salt thereof in the body of said mammal, which method comprises administering to said mammal in need of such prevention or treatment a pharmaceutically effective amount of an oligonucleotide analogue comprising two or more nucleoside units, wherein at least one of said nucleoside units is a structure of the formula (1a) of claim 11.

Claim 16. (withdrawn) The method according to claim 15, wherein the mammal is a human.

Claim 17. (withdrawn) A method for the prevention or treatment in a mammal of a disease preventable or treatable by the pharmacologically useful antigene activity of an oligonucleotide analogue or a pharmacologically acceptable salt thereof in the body of said mammal, which method comprises administering to said mammal in need of such prevention or treatment a pharmaceutically effective amount of an oligonucleotide analogue comprising two or more nucleoside units, wherein at least one of said nucleoside units is a structure of the formula (1a) of claim 11.

Claim 18 (original) The method according to claim 17, wherein the mammal is a human.

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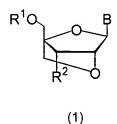
Claim 19. (withdrawn - currently amended) In an antisense oligonucleotide comprising two to one hundred nucleoside units, the improvement improvement comprising at least one of said nucleoside units having a structure of the formula (1a) of claim 11.

Claim 20. (withdrawn) In a probe for a gene comprising an oligonucleotide analogue, the improvement comprising the oligonucleotide analogue comprising two or more nucleoside units, wherein one of said units is a unit of the formula (1a) of claim 11.

Claim 21. (withdrawn) In a primer for starting amplification comprising an oligonucleotide analogue, the improvement comprising the oligonucleotide analogue comprising two or more nucleoside units, wherein one of said units is a unit of the formula (1a) of claim 11.

Claim 22. (withdrawn - currently amended) In an antisense antigene oligonucleotide comprising two to one hundred nucleoside units, the improvement comprising at least one of said units being a unit of the formula (1a) of claim 11.

Claim 23. (currently amended) A compound of the formula (1):



wherein R¹ represents a hydrogen atom or a protecting group for a hydroxy group;

 ${\ensuremath{\mbox{R}}}^2$ represents an azido group or an amino group that optionally is protected; and

B represents a purin-9-yl group or a pyrimidin-1-yl group, each of which optionally is unsubstituted or substituted with 1 or more substituents selected from the group consisting of

- a halogen atom
- an alkoxy group having from 1 to 6 carbon atoms,
- a hydroxyl group which may be protected,
- a mercapto group which may be protected,
- an amino group which may be protected,
- an alkoxy group having from 1 to 6 carbon atoms, a mono-alkylamino group, the alkyl group of which having 1 to 6 carbon atoms and a di-alkylamino group, the alkyl group of which has from 1 to 6 carbon atoms.

- Claim 24. (withdrawn) The compound according to claim 1, wherein the compound is 3'-azido-3'-deoxy-2'-O,4'-C-methylene-5-methyluridine.
- Claim 25. (withdrawn) The compound according to claim 1, wherein the compound is 3'-azido-5'-O-tert-butyldiphenylsilyl-3'-deoxy-2'-O,4'-C-methylene-5-methyluridine.
- Claim 26. (withdrawn) The compound according to claim 1, wherein the compound is 3'-azido-3'-deoxy-5'-O-(4,4'-dimethoxytrityl)-2'-O,4'-C-methylene-methyluridine.
- Claim 27. (withdrawn) The compound according to claim 1, wherein the compound is 3'-amino-3'-deoxy-5'-O-(4,4'-dimethoxytrityl)-2'-O,4'-C-methylene-5-methyluridine.
- Claim 28. (withdrawn) The compound according to claim 1, wherein the compound is 3'-amino-3'-deoxy-N(4-monomethoxytrityl)-2'-0,4-C-methylene-5-methyluridine-5-O-(2-cyanoethyl-N,N-disopropyl)-phosphramidite.